30. (Twice Amended) A cell transfected with a nucleic acid sequence, said nucleic acid sequence comprising a polynucleotide encoding at least on epitope, wherein said polynucleotide [(i) is capable of selectively hybridizing to, and (ii)] has at least [about 70%] 90% identity with a sequence selected from the group consisting of SEQUENCE ID NO 1; SEQUENCE ID NO 2; SEQUENCE ID NO 3; SEQUENCE ID NO 4; SEQUENCE ID NO 5; SEQUENCE ID NO 6; SEQUENCE ID NO 7; SEQUENCE ID NO 8; SEQUENCE ID NO 9; SEQUENCE ID NO 12; SEQUENCE ID NO 13[; fragments comprising at least about 10 nucleotides of any of SEQUENCE ID NOs 1, 2, 3, 4, 5;] and full complements thereof.

C4

38. (Twice Amended) A purified polynucleotide, [or a fragment comprising at least about 10 nucleotides thereof,] which codes for a polypeptide which comprises an amino acid sequence having at least [60%] 90% identity with SEQUENCE ID NO 24 or SEQUENCE ID NO 25.

C5

39. (Twice Amended) A purified polynucleotide comprising DNA having at least [50%] 90% identity with SEQUENCE ID NO 12 or SEQUENCE ID NO 13.

REMARKS

Claims 10-16, 25, 30, 35, 38-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility.

Applicant vigorously disagrees. CS141 is a previously unknown polynucleotide that codes for a protein 223 amino acid long and is useful as a diagnostic marker for diseases of the gastrointestinal (GI) tract due to its abundance in GI tissue.

Based on quantitative analysis of the occurrence of the CS141 polynucleotide in human breast tissue samples compared to human tissue samples representing the body as a whole, CS141 is approximately **12** times more abundant in gastrointestinal tract (GI) tissue than in the rest of the body. {Data are obtained from the Lifeseq database developed by Incyte Pharmaceuticals.} As is known scientists skilled in the cancer diagnostic arts, a gene product, such as a protein or messenger RNA (mRNA) coding for the protein, which is more prevalent and highly specific to one tissue type than other

tissue types, is extremely useful as a marker for the detection of disease in that tissue. If a protein appears in a tissue or body compartment where its normal occurrence is very low or non-existent, then the specific tissue in which the protein is normally found is in a diseased state. This is because the disease causes an alteration to the protein-specific tissue resulting in the protein escaping from its normal tissue into another. There are three main conditions which cause a tissue-specific protein to exist outside its specific host tissue: massive trauma, ischemia and hypertrophic proliferation. Thus, if a patient has not experienced a massive trauma or ischemia, detection of a tissue-specific protein outside that protein's host tissue indicates that the precise disease is hypertrophic proliferation of that tissue, the most serious form being cancer. There are many examples of the diagnostic use of tissue-specific protein markers. For instance, the appearance of prostate specific antigen (PSA) in seminal plasma is normal, but its detection in blood is indicative of prostate cancer. Further, the appearance of PSA messenger RNA (mRNA) in blood is indicative of prostate cancer. Likewise, the appearance of carcinoembryonic antigen (CEA) in colon and stool is normal, but its detection in blood at elevated levels is indicative of colorectal cancer. The attached Exhibit A illustrates the usefulness of tissue specific molecules which, upon detection in circulation, indicate proliferative disease. For Example, Exhibit A states that CEA is expressed in normal adult tissue but is detected in serum in patients with colorectal and other carcinomas. (p. 67, col. 2):

> *Some years after the discovery the same research group found that CEA could be measured in serum from patients with colorectal cancer and other carcinomas....[s]era from healthy individuals and from patients with other diseases generally had low levels of CEA... CEA assays are now generally accepted as a useful and cost-efficient tool in monitoring colon cancer...*

This journal article explains how a tissue specific molecule, expressed in the colon in normal individuals, is drained into lymph and blood vessels upon colon tumor growth. (Fig. 5)

In addition, the attached Declaration of Dr. Paula Friedman further proves the importance and usefulness of tissue-specific markers, such as CS141. In her Declaration, Dr. Friedman illustrates the similarities between well-known markers CEA and PSA and the novel CS141 when analyzed using the Incyte database. As shown, the tissue specificity of CS141 closely resembles the tissue specificity of the above mentioned

cancer markers. Clearly, the presence of CS141 outside of the GI tract illustrates cancer development of that tissue, just as the presence of CEA and PSA outside of their respective tissues indicates cancer of the colon and prostate, respectively. Thus, the above scientific facts support the utility of CS141 and illustrate that the appearance of CS 141 protein or mRNA in a patient blood sample is indicative of GI tract disease in that patient.

Thus, the above scientific facts support the utility of CS141 and illustrate that the appearance of CS141 protein or mRNA in a patient blood sample is indicative of proliferative gastrointestinal tract disease in that patient.

The Examiner is reminded of the proper standard under the Revised Interim Utility Guidelines which specifically states that utility is acceptable if it is "believable to a person of ordinary skill in the art based on the totality of the evidence and reasoning provided". The Guidelines continue stating "[A]n assertion is credible unless (a) the logic underlying the assertion is **seriously** flawed, or (b) the facts upon which the assertion is based are inconsistent with the logic underlying the assertion", (emphasis added). Simply put, the threshold to be met by Applicant is a **credible assertion** of utility, not the extraordinarily high threshold improperly held by the Examiner. Clearly, the appearance of a secreted CS141 gene product outside the gastrointestinal tract tissue itself, such as in whole blood, urine, stool or serum, indicates a form of gastrointestinal tract disease, akin to the presence of common markers such as PSA and CEA found in blood outside of their prevalent tissue type. CS141's use in diagnostic test in order to determine whether a patient has a disease of the GI tract unquestionably illustrates a credible utility.

Therefore, it is requested that this rejection be withdrawn.

Claims 10-16, 25, 30, 35, 38-43 are also rejected under 35 U.S.C. 112, first paragraph, by the Examiner who alleges the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Based on the aforementioned arguments made in response to the Examiner's 101 rejection, it is respectfully requested that this rejection be withdrawn.

Claims 10-16, 25, 30, 35 and 38-43 are rejected under 35 U.S.C. 112, first paragraph. Specifically, the Examiner states that the claims are drawn around polynucleotide sequences 70% (or 90%) identical to the polynucleotide sequences of SEQ ID NO:1-9, 12 OR 13, "fragments consisting of at least about 10 contiguous nucleotides of SEQ ID NO:1-5, polynucleotides that encode amino acid sequences 50% identical to SEQ ID NO:24-25 or fragments comprising at least about 8 contiguous amino acids of SEQ ID NO:24 or 25 and that none of these sequences meets the written description provision of 35 USC 112, first paragraph.

Due to the amendments to the claims which delete the fragment language, it is requested that this rejection be withdrawn.

Claims 10-16, 30, 35, 38, 40-43 are rejected under 35 U.S.C. 112, second paragraph. Specifically, claims 10, 11, 15 and 30 are vague and indefinite in the recitation "specifically binds."

Thus, Applicant has deleted this language from the claims.

Further, the Examiner states that claim 38 is vague and indefinite in the recitation "a fragment at least 10 nucleotides thereof, which codes for a polypeptide which comprises an amino acid sequence having at least 60% identity with SEQ ID NO:24 or SEQ ID NO:25."

Due to the fact that the Applicant has omitted this language from the claim, it is requested that this rejection be withdrawn.

The Examiner states sequences exactly identical to SEQ ID NO:1-9, 12, 13, 24, or 25 are not found in parent application 08/828,489, filed 3/31/97. Thus, for the application of the art, priority is granted only to the instant filing date, 3/31/98.

Applicant will clarify.

Claims 25 and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by 5,733,748 (filed 6/6/95). U.S. Patent 5,733,748 ('748 patent) discloses SEQ ID NO:6 which encodes the amino acid sequence SEQ ID NO:7, an amino acid sequence which is 100% identical to residues 89-223 of SEQ ID NO:24.

Since Applicant has deleted any fragment-type language from the claims and raised the percent identity, it is requested that this rejection be withdrawn.

CONCLUSION

In view of the aforementioned amendments and remarks, the aforementioned application is in condition for allowance and Applicant requests that the Examiner withdraw all outstanding objections and rejections and to pass this application to allowance.

Respectfully submitted,

P. A. Billing-Medel, *et al.*

Abbott Laboratories
D377/AP6D-2
100 Abbott Park Road
Abbott Park, IL 60064-6050
(847) 935-7550
Fax: (847) 938-2623

Mimi C. Goller
Registration No. 39,046
Attorney for Applicants